A Compensatory Subpopulation of Motor Neurons in a Mouse Model of Amyotrophic Lateral Sclerosis. By Schaefer AM, Sanes JR, Lichtman JW.

- **Aim:** To understand how loss and growth occur at individual neuromuscular junctions and whether such opposing events can occur in different branches of the same neuron or alternatively, whether whole motor units are either compensating or degenerative.
- **Methods:** Studied G93A SOD1/YFP (G93A SOD1 crossed with YFP expressing mice) and G93A SOD1 mice in which only a few motor axons were labeled. Immunostaining also done to boost YFP.
- **Results:** Diverse range of results observed at NMJ. Some junctions show no change others show varying degrees of change at different age points.
- **Conclusions:** Individual motor neuron pools of the transgenic mouse model of ALS have both losers and compensators.
- **BBQ:** What are the transient and enduring features of 'compensating' motor units versus 'degenerating' or 'dying-back' units and what mechanisms are responsible?

Early Vulnerability to Ischemia/reperfusion injury in motor terminals innervating fast muscles of SOD1-G93A Mice. By David G, Nguyen K and Barrett E.

- **Aim:** Analyse if motor terminals of G93A-SOD1 familial ALS or wild type mice were more vulnerable to I/R injury and if there is any difference between fast and slow twitch muscles.
- **Methods:** Used SOD1-G93A/YFP mice, Used only male mice for uniformity. Looked at the Soleus muscle, Extensor digitorum longus and plantaris muscle.
- **Results:** Motor terminals in EDL muscle of SOD1-G93A mice are highly sensitive to I/R injury, even at presymptomatic ages. Motor terminals innervating fast muscles are more sensitive to I/R injury than motor terminals innervating a slow muscle. EDL motor terminals in SOD1-G93A mice can re-sprout following I/R injury.
- **Conclusions:** Motor terminals innervating predominantly fast hindlimb muscles of mice expressing the G93A mutation of SOD1 are more vulnerable to I/R than the same terminals in wild-type mice.
- **BBQ:** What is the mechanism of I/R injury, the relevance to ALS, and why are fast unit more vulnerable?
The **WldS** Gene Modestly Prolongs Survival in the SOD1G93A fALS Mouse. By *Fischer et al*

- **Aim:** Analyse whether the WldS gene would both modify the neuropathology in the SOD1G93A mouse and similarly prolong its lifespan. Also investigate the effects of the disease progression in this mouse on its sensory neurons.
- **Methods:** SOD1G93A high expressing mice crossed with WldS mice to produce mice of 3 genotypes. Mice tested on rotapod apparatus. Medial gastrocnemius, soleus and tibialis anterior muscles were looked at.
- **Results:** Rotapod performance relatively similar between SOD/WT and SOD/WldS mice. Results showed sex dependence- 10 days difference between males and females
- **Conclusion:** Showed that the WldS gene did prolong survival, and a more pronounced difference was found in females than in males. Gene did show a protection against denervation of the motor endplate, it did not seem to protect the axon itself. The normal degeneration of the NMJ in the SOD/WldS mouse in older age is concurrent with data showing that the effect of the WldS protein decreases over time
- **BBQ:** Does WldS protein levels have to reach a threshold before it produces a neuroprotective effect, and could this be translated to humans?

Design, power, and interpretation of studies in the standard murine model of ALS. By *Scott et al*

- **Aim:** To test the controls in past studies and then replicate previous experiments with such agents using the same transgenic mice.
- **Methods:** SOD1G93A mouse model. Three different causes of deaths accounted for. Tail biopsy taken to prove presence of transgene. New controls used in this review study.
- **Results:** When retested with the new design none of the compounds previously found to extend the lifespan of the SOD1-G93A mouse had a significant effect.
- **Conclusion:** There are many flaws inherent to this model of ALS. The authors believe that the apparent efficacy of riluzole is due to a false negative or statistical error or may be too small to detect at the power of these studies. This may mean that the SOD1G93A mouse model is not a good representation of ALS.
- **BBQ:** Does the Scott et al study invalidate the SOD1 mouse as a model of human ALS?

(Group: Patrick Hillan, Charlie Carter, Charlie Carroll, Darren Woods and Rosie Saunderson)